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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/853,581	05/14/2001	Nabil Hanna	P 0280617 1997-30-0568A	7197

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EXAMINER	
NICKOL, GARY B	

ART UNIT	PAPER NUMBER
1642	

DATE MAILED: 03/24/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/853,581	HANNA ET AL.	
	Examiner	Art Unit	
	Gary B. Nickol Ph.D.	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *22 December 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *23-26,29,32-34 and 38-43* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *23-26,29,32-34 and 38-43* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *1/16/04; 12/22/03*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

Re: Hanna *et al.*

Date of priority: September 18, 1997

Response to Amendment

The Amendment filed December 22, 2003 in response to the Office Action of July 22, 2003 is acknowledged and has been entered.

Claims 23-26, 29, 32-34, 38-43 are currently under consideration.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office Action.

The species election between skin cancer, breast cancer, lung cancer, colon cancer, kidney cancer and prostate cancer is withdrawn in view of the newly cited reference below.

New Rejections/Objections:

Claim Objections:

Claim 29 is objected to because it depends from a cancelled claim (Claim 27). It is assumed, for examination purposes, that claim 29 depends from Claim 23.

Claims 38-42 are objected to under 37 CFR 1.75 as being substantial duplicates of claims 23-26 and 29. Independent claims 23 and 38 are both drawn to methods of treating cancer comprising administering (1) a composition that induce antigen-specific cytotoxic T-lymphocyte responses and (2) a composition that is an antagonist of an immunosuppressive factor. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper to object to the claims as being substantial duplicates. See MPEP § 706.03(k).

Claim Rejections:

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 32-33, 43 are rejected as vague and indefinite under 35 USC 112, 2nd paragraph. Specifically, Claim 32 recites the limitation *said* "cancer cells" (see step a). There is insufficient antecedent basis for this limitation in the claim.

Claim 43 recites the limitation *said* "antigen". There is insufficient antecedent basis for this limitation from which claim 43 depends. Claim 43 recites a vaccine which induces an *antigen-specific* CTL response. It's not clear if the limitations in Claim 43 refer to the vaccine or the CTL response.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 23-26, 29, 32-33, 34, 38-43 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The written description in this case only sets forth a method of treating cancer comprising administering the papilloma E7 protein in conjunction with anti-TGFβ antibodies. Thus, the written description is not commensurate in scope with the claims drawn to a vaccine composition comprising a genus of antigens (and or compositions) that induce an antigen-specific cytotoxic T-lymphocyte response *and* a genus of antagonists of immunosuppressive factors.

It is noted that the specification provides examples of a wide variety of known tumor associated antigens with regards to eliciting an antigen-specific CTL response (pages 13-14). The specification further acknowledges examples in the art of immunosuppressive factors, which can be secreted by tumor cells to avoid immune destruction (page 6). However, with regards to a method for treating cancer, the disclosure only *reasonably* conveys possession of an anti-cancer composition comprising anti-TGFβ antibodies in conjunction with E7-PROVAX™ (page 18, Figure 2A). The instant disclosure of a single species of antigen and antagonist fails to adequately describe the scope of the claimed genus of antagonists, and antigens (including those listed in Claims 33, 43). A description of a genus of antagonists or antigens may be achieved by

means of a recitation of a representative number of said antagonists or antigens, defined by structure, falling within the *scope* of the genus. However, the instant specification fails to provide sufficient descriptive information, such as definitive structural or functional features of the claimed genus of antagonists and antigens that would distinguish the claimed antagonists from other molecules that do not have the claimed biological properties. Since the disclosure fails to describe the common attributes or characteristics that identify members of the genus, and because the genus is highly variant, the disclosure of one specific peptide and related antibody is insufficient to describe the genus. Thus, one of skill in the art would reasonably conclude that the disclosure fails to provide a representative number of species to describe and enable the genus as broadly claimed.

Vas-Cath Inc. v. Mahurkar, 19USPQ2d 1111, clearly states "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed.*" (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See *Vas-Cath* at page 1116). As discussed above, the skilled artisan cannot envision the detailed chemical structure of the encompassed genus of antagonists, and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of isolating it. The compound itself is required. See *Fiers v. Revel*, 25 USPQ2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016.

One cannot describe what one has not conceived. See *Fiddes v. Baird*, 30 USPQ2d 1481 at 1483. In *Fiddes*, claims directed to mammalian FGF's were found to be unpatentable due to lack of written description for that broad class. The specification provided only the bovine sequence.

Therefore, only a method of treating cancer comprising administering the papilloma E7 protein in conjunction with anti-TGFβ antibodies , but not the full breadth of the claims, meets the written description provision of 35 U.S.C. §112, first paragraph. Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 U.S.C. §112 is severable from its enablement provision (see page 1115).

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 23-26, 29, 38-43 are rejected under 35 U.S.C. 102(e) as being anticipated by US Patent Application No. 2002/0004052 A1 (BERD *et al.*, June 7, 1995).

Berd *et al.* teach a method of treating cancer or neoplasms comprising the administration of a vaccine composition wherein said composition comprises the administration of an adjuvant composition that induces an antigen-specific cytotoxic T-lymphocyte response and an antagonist of an immunosuppressive factor. Specifically, Berd *et al.* teach the administration of tumor cells

or tumor cells extracts [para 41] which include antigens isolated from a hapten modified cancer cell or a cell membrane isolated from a hapten modified cancer cell. It is further noted that these peptides include a protein encoded by cancer oncogenes [para 42]. Berd *et al.* further teach the administration of an antagonist of an immunosuppressive factor administered sequentially or concurrently, and in any order with the adjuvant composition [para 46] wherein said antagonist is cyclophosphamide [para 9]. Further, as evidenced by Matar *et al.* (Eur. J. Cancer, May 2000, Vol. 36 No. 8, pages 1060-6), cyclophosphamide would effectively antagonize the immunosuppressive factor TGFβ. Berd *et al.* further teach wherein the CTL adjuvant composition is administered intradermally, intramuscularly or subcutaneously and the TGFβ antagonist is administered intravenously [para 47, and 96]. Berd *et al.* further teach various cancers that can be treated by the method, including melanoma, breast, lung, colon, kidney, and prostate cancers [para 40]. Further, although the prior art does not specifically teach the antigens listed in Claim 43, the administration of the melanoma cell vaccine as taught by Berd *et al.* would inherently induce an antigen-specific cytotoxic T-lymphocyte response specific for melanoma-associated antigens such as gp100, MART-1/MELAN A, MAGE, BAGE, etc. Thus, while Berd *et al.* do not specifically characterize the antigens to which the CTL response is directed at, the claimed functional limitation would be an inherent property of the referenced method since the specification discusses (page 13) a wide variety of melanoma associated antigens. Thus, it does not appear that the claim language or limitation results in a manipulative difference in the method steps when compared to the prior art disclosure. See Bristol-Myers Squibb Company v. Ben Venue Laboratories 58 USPQ2d 1508 (CAFC 2001).

Claim Rejections - 35 USC § 103

Claims 23-26, 29, 32-34, 38-43 are rejected under 35 U.S.C. 103(a) as being unpatentable over Raychaudhuri *et al.* (US Patent No. 5,695,770, June 1995, IDS) in combination with the teachings of Patent Application No. 2002/0004052 A1 (BERD *et al.*, June 7, 1995) and Berd *et al.* (Cancer Research, Vol. 46, May 1986, pages 2572-2577).

1. Raychaudhuri *et al.* teach methods of treating neoplastic or cancerous growths (column 6, line 26) comprising administering to a patient an admixture comprising a cancer or tumor antigen expressed by said cancer in an amount sufficient to induce a cytotoxic T-lymphocyte response (abstract) wherein said antigen formulation comprises and a microfluidized antigen formulation comprising a stabilizing detergent, a micelle-forming agent, and a biodegradable and biocompatible oil wherein said antigen formulation is formulated as a stable oil-in-water emulsion (column 4, lines 29+) Raychaudhuri *et al.* further teach that said antigen is selected from the group consisting of papillomavirus E7 protein (column 6, lines 4-5; column 20, lines 45+).
2. Raychaudhuri *et al.* do not teach the antigen formulation above *in combination* with a therapeutically effective amount of at least one agent which is capable of neutralizing or down regulating the activity of tumor and host-secreted immunosuppressive factors.

3. Berd *et al.* teach compositions and methods for treating cancer comprising adminstering vaccine compositions that induce antigen-specific cytotoxic T-lymphocyte responses (see teachings of Berd *et al.* above). Further, Berd *et al.* teach that the combination of low dose cyclophosphamide and vaccine can produce clinically important regression of metastatic tumor [para 0009]. In fact, it has been well known in the art that adjuvant administration of cyclophosphamide markedly augments the development of delayed-type hypersensitivity (DTH) to melanoma-associated antigens and that the resultant immunity can cause regression of metastatic tumors (Berd *et al.*, Cancer Research, Vol. 46, May 1986, pages 2572-2577).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to augment or optimize the cancer vaccine of Raychaudhuri *et al.* by including the administration of cyclophosphamide. One would have been motivated to do so because it was well known in the art at the time the invention was made that that the combination of low dose cyclophosphamide and vaccine can produce clinically important regression of metastatic tumor. Further, one of ordinary skill in the art would have had a reasonable expectation that cyclophosphamide would augment the anti-tumor immunity based on the successful teachings of Berd *et al.* (Cancer Research, Vol. 46, May 1986, pages 2572-2577) who demonstrated that the DTH responses of patients who received the combination of cyclophosphamide and vaccine versus controlled patients (vaccine only) was significantly greater (see abstract).

No claim is allowed.

All other rejections and or objections are withdrawn in view of applicant's amendments and arguments there to.

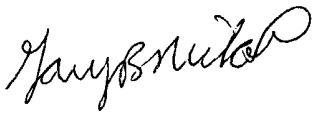
Any inquiry concerning this communication or earlier communications from the examiner should be directed to Gary B. Nickol Ph.D. whose telephone number is 571-272-0835. The examiner can normally be reached on M-Th, 8:30-5:30; alternate Fri., 8:30-4:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne Eyler can be reached on 571-272-0871. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Gary B. Nickol Ph.D.
Primary Examiner
Art Unit 1642

March 22, 2004



GARY NICKOL
PRIMARY EXAMINER